

promotes *hedgehog* signal transduction, and (b) is encodable by a nucleic acid sequence designated in SEQ ID NO: 4, SEQ ID NO: 6, or an N-terminal fragment of at least 150 contiguous nucleotides thereof.

4. **(Four Times Amended)** A method for the treatment of cerebral ischemia which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cerebral ischemia, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is encodable by a nucleic acid sequence designated in SEQ ID NO: 4, SEQ ID NO: 6, or an N-terminal fragment of at least 150 contiguous nucleotides thereof.

5. **(Four Times Amended)** A method for the treatment of stroke which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to treat stroke, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is encodable by a nucleic acid sequence designated in SEQ ID NO: 4, SEQ ID NO: 6, or an N-terminal fragment of at least 150 contiguous nucleotides thereof.

6. **(Four Times Amended)** A method for the treatment of transient ischemia attack which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cell damage caused by a transient ischemic attack, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is encodable by a nucleic acid sequence designated in SEQ ID NO: 4, SEQ ID NO: 6, or an N-terminal fragment of at least 150 contiguous nucleotides thereof.

18. **(Reiterated)** The method of claim 5, wherein the stroke is a thrombotic stroke.

19. **(Reiterated)** The method of claim 5, wherein the stroke is an embolic stroke.

22. **(Reiterated)** The method of any of claims 3-6, wherein the patient is treated prophylactically.
26. **(Amended)** The method of any of claims 3-6, further comprising administering one or more of an anticoagulant, an antiplatelet agent, a thrombin inhibitor, and/or a thrombolytic agent.
27. **(Amended)** The method of any of claims 3-6, further comprising performing vascular surgery.
28. **(Reiterated)** The method of claim 27, wherein the vascular surgery comprises carotid endarterectomy.
40. **(Amended)** A method for the treatment of cerebral infarctions which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cerebral infarct volume, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to SEQ ID NO: 13, SEQ ID NO: 15, or an N-terminal fragment of at least 50 contiguous amino acids thereof.
41. **(Amended)** A method for the treatment of cerebral ischemia which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cerebral ischemia, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to SEQ ID NO: 13, SEQ ID NO: 15, or an N-terminal fragment of at least 50 contiguous amino acids thereof.
42. **(Amended)** A method for the treatment of stroke which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to treat stroke, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to SEQ ID NO: 13, SEQ ID NO: 15, or an N-terminal fragment of at least 50 contiguous amino acids thereof.

43. (Amended) A method for the treatment of transient ischemia attack which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cell damage caused by a transient ischemic attack, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to SEQ ID NO: 13, SEQ ID NO: 15, or an N-terminal fragment of at least 50 contiguous amino acids thereof.

44. (Amended) A method for the treatment of cerebral infarctions which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide and at least one additional agent, in an amount effective to reduce cerebral infarct volume, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to SEQ ID NO: 13, SEQ ID NO: 15, or an N-terminal fragment of at least 50 contiguous amino acids thereof, and wherein said additional agent is selected from at least one of an anticoagulant, an antiplatelet agent, a thrombin inhibitor, or a thrombolytic agent.

45. (Amended) A method for the treatment of cerebral ischemia which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide and at least one additional agent, in an amount effective to reduce cerebral ischemia, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to SEQ ID NO: 13, SEQ ID NO: 15, or an N-terminal fragment of at least 50 contiguous amino acids thereof, and wherein said additional agent is selected from at least one of an anticoagulant, an antiplatelet agent, a thrombin inhibitor, or a thrombolytic agent.

46. (Amended) A method for the treatment of stroke which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide and at least one additional agent, in an amount effective to treat stroke, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to SEQ ID NO: 13, SEQ ID NO: 15, or an N-terminal fragment of at least 50 contiguous amino acids thereof, and wherein said additional

agent is selected from at least one of an anticoagulant, an antiplatelet agent, a thrombin inhibitor, or a thrombolytic agent.

47. **(Amended)** A method for the treatment of cerebral infarctions which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cerebral infarct volume, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to SEQ ID NO: 13, SEQ ID NO: 15, or an N-terminal fragment of at least 50 contiguous amino acids thereof, and wherein said method additionally includes surgery.

48. **(Amended)** A method for the treatment of cerebral ischemia which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cerebral ischemia, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to SEQ ID NO: 13, SEQ ID NO: 15, or an N-terminal fragment of at least 50 contiguous amino acids thereof, and wherein said method additionally includes surgery.

49. **(Amended)** A method for the treatment of stroke which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to treat stroke, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to SEQ ID NO: 13, SEQ ID NO: 15, or an N-terminal fragment of at least 50 contiguous amino acids thereof, and wherein said method additionally includes surgery.

<i>The claims presented above incorporate changes as indicated by the marked-up versions below.</i>

3. **(Four Times Amended)** A method for the treatment of cerebral infarctions which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an

amount effective to reduce cerebral infarct volume, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is encodable by a nucleic acid ~~that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid~~ sequence designated in ~~at least one of~~ SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, or an N-terminal fragment of at least 150 contiguous nucleotides thereof.

4. **(Four Times Amended)** A method for the treatment of cerebral ischemia which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cerebral ischemia, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is encodable by a nucleic acid ~~that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid~~ sequence designated in ~~at least one of~~ SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, or an N-terminal fragment of at least 150 contiguous nucleotides thereof.

5. **(Four Times Amended)** A method for the treatment of stroke which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to treat stroke, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is encodable by a nucleic acid ~~that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid~~ sequence designated in ~~at least one of~~ SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6, or an N-terminal fragment of at least 150 contiguous nucleotides thereof.

6. **(Four Times Amended)** A method for the treatment of transient ischemia attack which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cell damage caused by a transient ischemic attack, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is encodable by a nucleic acid ~~that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a~~

~~nucleic acid~~ sequence designated in ~~at least one of SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6,~~ or an N-terminal fragment of at least 150 contiguous nucleotides thereof.

26. (Amended) The method of any of claims ~~1 and 3-6,~~ further comprising administering one or more of an anticoagulant, an antiplatelet agent, a thrombin inhibitor, and/or a thrombolytic agent.

27. (Amended) The method of any of claims ~~1 and 3-6,~~ further comprising performing vascular surgery.

40. (Amended) A method for the treatment of cerebral infarctions which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cerebral infarct volume, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is ~~at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or~~ an N-terminal ~~a bioactive~~ fragment of at least 50 contiguous amino acids thereof.

41. (Amended) A method for the treatment of cerebral ischemia which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cerebral ischemia, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is ~~at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or~~ an N-terminal ~~a bioactive~~ fragment of at least 50 contiguous amino acids thereof.

42. (Amended) A method for the treatment of stroke which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to treat stroke, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is ~~at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or~~ an N-terminal ~~a bioactive~~ fragment of at least 50 contiguous amino acids thereof.

43. (Amended) A method for the treatment of transient ischemia attack which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cell damage caused by a transient ischemic attack, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is ~~at least 80% identical to at least one of SEQ ID NO: 10, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, or an N-terminal a-~~ an N-terminal a- bioactive fragment of at least 50 contiguous amino acids thereof.

44. (Amended) A method for the treatment of cerebral infarctions which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide and at least one additional agent, in an amount effective to reduce cerebral infarct volume, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to ~~encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in at least one of SEQ ID NO: 1, SEQ ID NO: 134, SEQ ID NO: 5, or SEQ ID NO: 156, or an N-terminal fragment of at least 50 contiguous amino acids thereof,~~ and wherein said additional agent is selected from at least one of an anticoagulant, an antiplatelet agent, a thrombin inhibitor, or a thrombolytic agent.

45. (Amended) A method for the treatment of cerebral ischemia which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide and at least one additional agent, in an amount effective to reduce cerebral ischemia, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to ~~encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in at least one of SEQ ID NO: 1, SEQ ID NO: 134, SEQ ID NO: 5, or SEQ ID NO: 156, or an N-terminal fragment of at least 50 contiguous amino acids thereof,~~ and wherein said additional agent is selected from at least one of an anticoagulant, an antiplatelet agent, a thrombin inhibitor, or a thrombolytic agent.

46. (Amended) A method for the treatment of stroke which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide and at least one additional agent, in an amount effective to treat stroke, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in at least one of SEQ ID NO: 1, SEQ ID NO: 134, SEQ ID NO: 5, or SEQ ID NO: 156, or an N-terminal fragment of at least 50 contiguous amino acids thereof, and wherein said additional agent is selected from at least one of an anticoagulant, an antiplatelet agent, a thrombin inhibitor, or a thrombolytic agent.

47. (Amended) A method for the treatment of cerebral infarctions which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cerebral infarct volume, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in at least one of SEQ ID NO: 1, SEQ ID NO: 134, SEQ ID NO: 5, or SEQ ID NO: 156, or an N-terminal fragment of at least 50 contiguous amino acids thereof, and wherein said method additionally includes surgery.

48. (Amended) A method for the treatment of cerebral ischemia which comprises systemically administering to a patient in need thereof a *hedgehog* polypeptide in an amount effective to reduce cerebral ischemia, wherein said *hedgehog* polypeptide comprises an amino acid sequence that (a) binds to a naturally occurring *patched* receptor and promotes *hedgehog* signal transduction, and (b) is identical to encodable by a nucleic acid that hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in at least one of SEQ ID NO: 1, SEQ ID NO: 134, SEQ ID NO: 5, or SEQ ID NO: 156, or an N-terminal fragment of at least 50 contiguous amino acids thereof, and wherein said method additionally includes surgery.